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Refer to: Goldstein E, Hoeprich PD: Lymphangiography in diagnosis of fever of unknown origin. Calif Med 119:59-61, Nov 1973

Lymphangiography in Diagnosis of Fever of Unknown Origin

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WHEN FEVER PERSISTS and the cause remains unknown despite extensive evaluation, surgical exploration of the abdomen is frequently recommended for diagnosis.[1-4] This procedure has considerable merit because intra-abdominal processes that may cause fever—for example, lymphomas of the retroperitoneal space[3,5] are frequently occult. However, there are many extra-abdominal causes for persistent fevers that are quite important (among them tuberculosis, subacute bacterial endocarditis, polyarteritis) and these may also elude early diagnosis. As a result, the decision to operate and the timing of the operation are clinical judgments which are exceedingly difficult. We recently performed lymphangiography as part of the preoperative evaluation of a patient with a persistent fever. Because such use of lymphangiography has been reported infrequently,[3,6] we report our experience to emphasize the value of this procedure in the early diagnosis of fever of unknown origin.

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Submitted April 3, 1973.

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Report of a Case

A 55-year-old male agronomist was referred to the Sacramento Medical Center in April 1972 for evaluation of fever and fatigue of two months' duration. With the exception of these symptoms the history was unremarkable. On physical examination the patient was observed to be chronically ill-appearing, the temperature was 39.8°C (103.6°F), blood pressure 130/80 mm of mercury and pulse rate 108 per minute. A non-pruritic maculopapular rash was present over the chest and abdomen. There was no palpable enlargement of lymph nodes, liver or spleen.

Laboratory studies showed a hematocrit of 35, a leukocyte count of 5,100 per cu mm with 49 percent polymorphonuclear neutrophils, 32 percent lymphocytes, 18 percent monocytes, and 1 percent eosinophiles. The platelet count was 155,000 per cu mm. The erythrocyte sedimentation rate was 53 mm in one hour (Wintrobe). Results of urine and cerebrospinal fluid examinations were normal. Blood chemistry determinations, including glutamic oxaloacetic transaminase (SGOT), alkaline phosphatase, lactic dehydrogenase, bilirubin, albumin, globulin, urea nitrogen, uric acid and haptoglobin were within normal limits. Antinuclear antibody, rheumatoid factor tests, direct and indirect Coombs tests, the VDRL test and serum protein electrophoresis were negative. The feces was guaiac-negative. An electrocardiogram was normal.

No abnormalities were noted in roentgenological examinations of the chest, skull, esophagus, stomach, subphrenic space, small intestine, large intestine, gall bladder, and common bile duct. An intravenous pyelogram revealed a horseshoe kidney. A radionuclide scan of the liver was normal. Skin tests with coccidioidin, intermediate strength tuberculin, histoplasmin, and mumps antigen were nonreactive. Agglutinins for typhoid O, typhoid

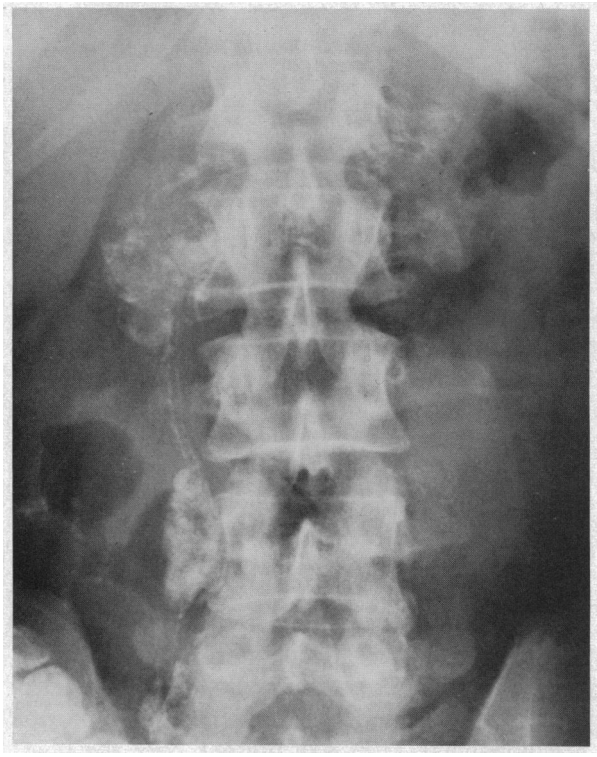

Figure 1.—Lymphangiogram showing enlarged para-aortic lymph nodes which are foamy in appearance and contain filling defects.

H, paratyphoid A, paratyphoid B, Pasteurella tularensis and Brucella abortus were negative, as were blood smears for malaria, and examination of feces for ova and parasites. Cultures of blood, and urine were sterile. A biopsy of bone marrow was interpreted as showing granulocytic hyperplasia. A liver biopsy (Menghini) showed no abnormality. Chronic inflammation was noted in a biopsy specimen from the maculopapular skin rash. Cultures of the biopsy material did not grow either nonacid-fast or acid-fast bacteria, or fungi.

Lymphangiography on the tenth hospital day disclosed enlarged para-aortic abdominal lymph nodes which were compatible in appearance with malignant lymphoma (Figure 1). Abdominal laparotomy was carried out three days later. Biopsy specimens from the enlarged lymph nodes which lay beneath the horseshoe kidney were diagnostic of Hodgkin's disease. The tumor was also present in a liver biopsy specimen and in the excised spleen.

Postoperatively, the patient continued to have high spiking fevers. He was treated with methyl prednisolone, cycloposphamide, vincristine, and procarbazine. After transient improvement, leukopenia developed with fewer than 300 white blood cells per cu mm—all lymphocytes. Despite treatment with gentamicin (1.7 mg per kg of body weight every 8 hours, intravenously) and carbenicillin (400 mg per kg of body weight per day by continuous intravenous infusion) the patient died of pneumonia. Pseudomonas aeruginosa and Escherichia coli grew on cultures of the fluid.

The significant findings at autopsy were Hodgkin's disease involving the bone marrow, liver, and lymph nodes (pelvic, abdominal thoracic, cervical). There was agranulocytosis of the bone marrow and five-lobe, hemorrhagic bacterial pneumonia caused by P. aeruginosa and E. coli (susceptible, by *in vitro* testing, to gentamicin and carbenicillin).

Discussion

This case illustrates the value of lymphangiography in evaluating fever of occult origin. The roentgenographic features were sufficiently distinctive to predict that a lymphoma involving the para-aortic lymph nodes would be found at laparotomy. However, additional experience is needed to assess the reliability of the procedure. It is likely that falsely positive results occur due to nonspecific lymphadenitis[8] or to other neoplasms.[9] Of equal concern is the possibility of falsely negative results—a possibility that is real but apparently small with lymphoma.[7,8] Although these potential sources for error exist, the high degree of correlation between positive histologic and radiographic findings—more than 80 percent—suggests that the technique will be diagnostically reliable.

The major hazard from lymphangiography is the rare occurrence of an oil embolus.[10,11] Absolute or relative contraindications are few; they include parenchymal pulmonary disease, a patent foramen ovale and allergy to iodine.[8]

Lymphangiography is also of value in localizing the site of lymph node involvement. In our patient, the lymphangiogram located grossly diseased nodes beneath the horseshoe kidney enabling the surgeon to select an appropriate site for biopsy.

Summary

Lymphangiography of the retroperitoneal lymphatic system was performed early in the evaluation of a patient with a persistent fever of unknown cause. The roentgenograms demonstrated enlarged para-aortic lymph nodes which were compatible in appearance with a malignant lymphoma. Abdomi-

nal laparotomy confirmed the preoperative diagnosis.

Retroperitoneal lymphangiography is recommended as a useful procedure in the preoperative evaluation of patients with persistent fevers of unknown cause.

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